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EFFECT OF FLAXSEEDS ON ISOPROTERENOL INDUCED CARDIOTOXICITY IN RATS

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ABSTRACT

The present study was performed to explore the potential effects of flaxseed against isoproterenol induced cardiotoxicity in rats. Forty rats classified into control negative group and isoproterenol induced cardiac toxicity (85 mg/kg body weight) four rat groups that reclassified into untreated control positive and flaxseed powder, oil and extract treated rat groups. The study was assigned for 60 day. Administration of flaxseed either in form of powder, oil and extract improve of nutritional indicator (weight gain, food efficiency ratio and protein efficiency ratio) reducing hyperlipidemia (lower serum total cholesterol, LDLc, VLDLc and elevate HDLc), decline in atherogeneses (total cholesterol/ HDLc) normalize values of liver parameters (cholesterol, T. lipids, TG, ALT, AST, ALP and LDH) and antioxidant markers (SOD and catalase along with significant lower in the level of malondialdehyde, cardiac XO, LDH and NO). It can be concluded that the administration flaxseed powder, oil or extract can lower the side effects of isoproterenol induced cardiotoxicity in rats and reducing the risk factors for cardiovascular disease such as hyperlipidemia, leakage of cardiac markers and nutritional indicators.

KEYWORDS: Isoproterenol- flaxseeds- hyperlipidemia- cardiac marker-rats.

INTRODUCTION

Cardiovascular Disease remains the principal cause of death in both developed and developing countries. It may present as a typical `heart attack', as sudden death, or it may be detected at an advanced stage and be described as a silent infarct. Increasing level of lipid leads to cardiovascular diseases and stroke that are a major cause of morbidity and mortality

all over the world. Hyperlipidemia contributes significantly in the prevalence and severity of atherosclerosis and coronary heart diseases **(Gupta and Jain, 2009 and Gosain et al., 2010)**. Increased LDL cholesterol undergoes oxidative modification in the presence of free radicals **(Saradha and Jhan 2009)**. Isoproterenol, ISO, [1-(3,4-dihydroxyphenyl)-2-isopropylamino ethanol hydrochloride] induced cardiotoxicity in rats which is one of the most widely accepted models **(Kavya and Kumar 2016)**. Isoproterenol is a chemically synthesized catecholamine and β-adrenergic agonist, which causes severe stress to the myocardium leading to infarct like necrosis **(Wang et al., 2016)**. Catecholamine produced from ISO generates free radicals that induce cardiotoxicity. Compromised antioxidant resistance leads to metabolic and contractile impairments and alteration in the membrane permeability consequent to lipid peroxidation and irreversible damage to the myocardial membrane **(Evran et al., 2014 and Liaudet et al., 2014)**. Scientists and researcher are trying to substitute herbal plant and some natural component in these plants for treatment of cardiovascular diseases because of highly cost synthetic drugs and probable drugs side effects **(Hajizadeh** and **Mirzajani 2011)**. It is well known that flaxseed *(Linum usitatissimum)* is an oilseed and is a good source of oil, protein and dietary fiber as well as the phytochemical antioxidant **(Daun et al., 2003)**. Flaxseeds have also received increasing attention for their potential role in preventing lipid disorders.

The present work aimed to investigate alleviating effect of flaxseeds administration on isoproterenol induced cardiotoxicity in rats.

MATERIALS AND METHODS

A – Materials

1- Chemicals

Isoproterenol hydrochloride was purchased from Sigma Chemical Company St.Louis, MO, and USA. All of the other chemicals and kits used were of analytical grade.

2-Flaxseeds

Flaxseeds *(Linum usitatissimum L.)* were purchased from Agricultural Seeds, Medicinal Plants and Herbs Company, Cairo, Egypt.

3-Albino rats

Forty adult albino rats weighing around 140± 6g were purchased from experimental animals' center in Medicine collage of King Saud University in Riyadh. The animal use protocol had

been approved by the Institutional Animals Ethics Committee. The animals were housed in cages maintained under suitable conditions of temperature (25 ± 1°C), humidity (60 ± 10%), ventilation (continuous circulation of fresh air), and illumination (a 12 hours dark and 12 hours light cycle). Standard diet was prepared according to **NRC (1995**). Rats were kept under observation for five days before experiment and fed on standard diet and water *ad-libitum*.

B- Methods

1- Preparation of flaxseeds powder and oil

Flaxseeds were washed with tap water to remove possible potential dust and exposed to air-circulated oven at 40°C to complete dryness then grinded to fine powder and given to rats at 15% of standard diet. Flaxseeds oil was obtained by solvent extraction with petroleum ether (Merck, 40-60°C) in Sox let apparatus and the remaining solvent was removed by distillation. After extraction, the oil samples were filtered and stored. Extracted oil samples had a light yellow color and very characteristic flavor. Flaxseeds oil rat dose was 5% in diet in substitution of corn oil of standard diet.

2- Hydroalcoholic extract preparation

100 g of flaxseeds were macerated in 11 ml of methanol at room temperature overnight, filtered and crude extract was collected then repeat with another 11 ml of methanol on flaxseeds residue under refluxing in a water bath for 2 hours and then filtered. The filtrate was collected. Another 1 l volume of distilled water was added to the residue, boiled for 2 hours under the reflux condenser, and filtered. The hot water filtrate was added to the previous crude extract to form the hydroalcoholic crude extract which evaporated to dryness under reduced pressure at 60°C and then kept in dark bottles and stored in a deep freezer until usage according to **Charles et al., (1993)**. The rat dose was 500 mg/kg body weight by stomach tube.

3-Estimation of flaxseeds phenolic content and antioxidants activity

High-performance liquid chromatography (HPLC) analysis of extracts was performed using an Agilent 1200 chromatograph was selected for detection described by the method of **Goupy et al., (1999)**.

4- Induction of cardiotoxicity in rats

Induction of cardiotoxicity in rats was induced by subcutaneous injection of freshly prepared solution of isoproterenol hydrochloride at dose 85 mg/kg body weight in cold saline for two days according to **Goyal et al., (2009)**.

5- Animal treatments

Rats classified into control negative group and ISO induced cardiac toxicity four rat groups that reclassified into untreated control positive, and flaxseed powder, oil and extract treated rat groups. The study was assigned for 60 day. The food intake was calculated daily and the body weight gain was recorded weekly.

6-Sample preparation

Blood samples were obtained from the orbital sinus using capillary tubes under mild ether anesthesia. Blood for hematology studies was collected into tubes then rats were sacrificed and the liver and heart were immediately removed, washed three times in ice cold saline and blotted on ash-free filter paper, then used for preparation of tissue homogenates.

7-Determination of some of serum biochemical parameters

Serum alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and LDH were estimated according to **Rietman and Frankel, (1957), Bessey et al., (1946) and Esher et al., (1973),** respectively. Estimation of serum total cholesterol(CHO), triglyceride (TG), high density lipoprotein cholesterol (HDLc), low density lipoprotein cholesterol (LDLc) and total lipids (T.lipids) were estimated by using the spin react enzymatic kits according to **Richmond (1973), Buccolo and David (1973), Grodon and Amer (1977) and Folch et al.,(1957),** respectively. Serum superoxide dismutase (SOD), catalase (CAT), and malodialdehyde (MDA) were estimated according to **Misra and Fridovich (1972), Cohen et al., (1970)** and **Draper and Hadley (1990),** respectively.

Determination of some of liver and cardiac biochemical parameters

The liver and heart of each rat was homogenized in cold KCl solution (1.5%) to give a 10% homogenate. Liver total cholesterol (CHO), triglyceride (TG) total lipids (T. lipids) were estimated according to **Richmond (1973), Scheletter and Nussel (1975) and Folch et al., (1957)**, respectively. Cardiac markers as lactatet dehydrogenase (LDH), nitric oxide (NO) and Xanthine oxidase (XO) were estimated according to **Caband and Wroblewski (1958)**,**Williams (1984**) and **Bergmever (1974))**, respectively.

8-Calculation of some parameters

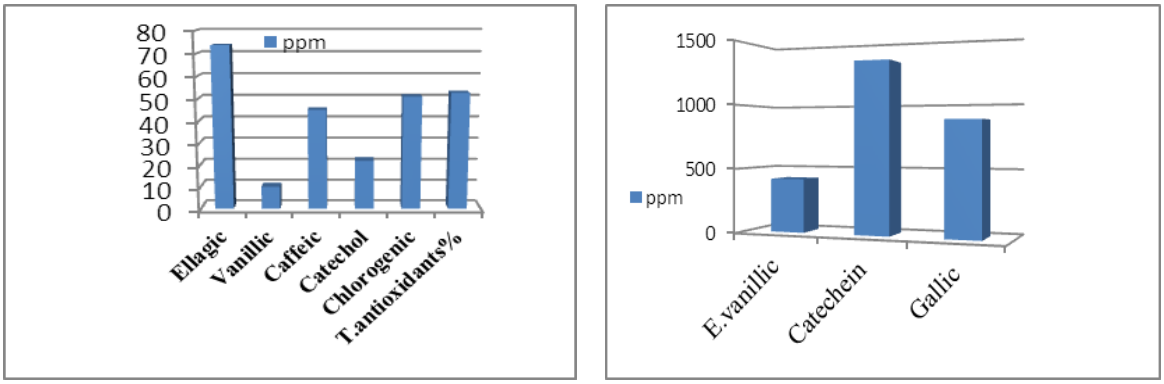
Feed efficiency ratio and protein efficiency ratio were determined according to the method of **Chapman et al., (1950**). Very low density lipoprotein (VLDLc) was calculated (VLDL-c = TG/ 5) according **Friedwald et al., (1972**). Atherogenic index (CHO/HDLc) was calculated according to **Castelli and levitar (1977)**.

Statistical analysis

All the obtained data were statistically analyzed by SPSS computer soft ware. The calculated occurred by analysis of variance ANOVA and follow up test LSD by SPSS ver.11 according to **Artimage and Berry (1987)**.

RESULTS AND DISCUSSION

Figure (1): Phenolic constituents of flaxseed and total antioxidants.



It is well known that phenolic compounds form a substantial part of plant foods and a vital role in the development of various human diseases including cardiovascular diseases because of these phenolic compounds are antioxidants *in vitro* and antioxidants **(Kumaran and Prince 2010)**. The flaxseed powder have higher value of phenolic compound as E.vanillic, Catechein and gallic as values being 417.55,1330.77 and 880.33 ppm respectively and also have ellagic, vanillic, caffeic, catechol, chlorogenic as values being 73.66, 10.11, 45.17, 22.11 and 51.12 ppm. The total antioxidant was 52.77 % as illustrated in figure 1. The difference in these values from previous researcher was related to the methods of estimation, genotype and the variety of flaxseeds in different countries **(Cui et al., 1996)**. The obtained results agreed with the results of **Westcott et al. (2000); Eliasson *et al.* (2003)**, **Mueller et al., 2010 and Tanvir et al., 2015** who demonstrated that flaxseed powder has P-coumaric, Ferulic, Caffeic, Gallic acid, traces of 4-hydroxybenzoic acid and O- glycosides. Phenolic acids such as gallic acid, syringic acid, vanillic acid, and p-coumaric acid and flavonoids such as catechin and naringenin are important constitutive antioxidants found in flaxseed. **Siger et**

al., (2008) recorded that four phenolic acids identified in defatted flaxseed powder are ferulic acid (10.9 mg/g), chlorogenic acid (7.5 mg/g), gallic acid (2.8 mg/g), and traces of 4-hydroxybenzoic acid. The major flavonoids in flax are flavone C- and O- glycosides.

Table (1): Nutritional indicators of normal control and isoproterenol induced cardiotoxicity rat groups treated with flaxseed powder, oil and extract at the end of the experimental period.

Groups	BWG (g)	BWG%	FI (g)	PI (g)	PER	FER
Control negative	70.31± 4.51a	50.11± 3.22a	18.77± 1.77a	3.77± 0.66a	0.31± 0.01a	0.062± 0.003a
Control positive	46.77± 4.22b	33.12± 2.75c	15.76± 1.33b	3.11± 0.88a	0.25± 0.03c	0.049± 0.004c
Flaxseed powder	67.65± 6.33a	46.68± 3.10a	18.16± 1.81a	3.64± 0.56a	0.30± 0.02a	0.062± 0.001a
Flaxseed oil	65.33± 4.61a	44.97± 3.65b	18.33± 1.25a	3.67± 0.44a	0.29± 0.01ab	0.059± 0.005b
Flaxseed extract	66.77± 4.75a	46.44± 3.61ab	18.25± 1.66a	3.68± 0.58a	0.30± 0.01a	0.060± 0.002ab

Mean values in each column having different superscript (a,b,c&d) are significantly different at P <0.05 Body weight gain (BWG) food intake (FI) protein intake (PI) protein efficiency ratio (PER) and food efficiency ratio (FER).

Feeding and growth performance in terms of BWG, BWG%, FI, PI, PER, and FER of control negative, control positive and myocardial necrosis rat groups treated with flaxseed powder, oil and extract were presented in table (1). In comparing with control negative group, the myocardial necrosis control positive group showed significant decrease in BWG, BWG%, FI, PER, and FER. ISO induced cardiotoxicity rat groups treated with flaxseed powder, oil and extract showed significant increase in these parameters when compared with control positive group and non significant difference when compared with control negative group except rat group treated with flaxseed oil which showed significant decrease of BWG % and FER of compared with control negative group.

The improvement of nutritional indicators in rats administrated flaxseeds may be attributed to the biologically active components as omega-3, digestible proteins, and lignans. In addition to being one of the richest sources of α-linolenic acid oil and lignans, flaxseed is an essential source of high quality protein and soluble fiber and has considerable potential as a source of phenolic compounds **(Oomah 2001 and Pengilly 2003)**. The amino acid pattern of flax protein is similar to that of soybean protein and has a favorable ratio of amino acids with

Lysine, Threonine and Tyrosine as the limiting amino acids. Furthermore, it is a good source of sulfur amino acids as methionine and cysteine and also of branched chain amino acids as isoleucine, leucine and valine. Flaxseed is reach in essential amino acids of great importance in the synthesis of proteins that have the role of maintenance and repair of cells, tissues and organs **(Rabetafika et al.,2011)**. Flaxseed has large number of bioactive photochemical that has beneficial effect on the cardiovascular disease by virtue of their lipid lowering, antinational, antioxidant and cardioprotective effects **(Dwivedi 2004)**.

Table (2): Serum lipids pattern of normal control and isoproterenol induced cardiotoxicity rat groups treated with flaxseed powder, oil and extract at the end of the experimental period.

Groups	TC (mg/dl)	TG (mg/dl)	HDLc (mg/dl)	LDLc (mg/dl)	VLDLc (mg/dl)	T. lipids (mg/dl)	CHO/HDLc
Control negative	103.77± 12.66bc	97.66± 10.22bc	38.11± 5.01a	46.13± 5.65c	19.53± 2.80c	335.11± 63.44c	2.72± 0.50bc
Control positive	290.61± 39.66a	170.60± 25.67a	25.11± 3.66c	231.38± 60.66a	34.12± 4.77a	778.11± 150.33a	11.57± 2.77a
Flaxseed powder	122.14± 20.66b	119.33± 15.11b	31.61± 4.77b	66.67± 6.77b	23.86± 3.10bc	395.77± 80.44b	3.54± 0.55b
Flaxseed oil	118.66± 17.21b	120.70± 14.77b	33.75± 4.61ab	60.77± 6.07b	24.14± 3.51b	390.82± 75.33bc	3.51± 0.65b
Flaxseed extract	115.77± 14.71b	113.55± 12.45b	34.29± 4.66a	58.77± 6.11b	22.71± 3.11bc	382.55± 71.11bc	3.37± 0.76b

Mean values in each column having different superscript (a, b, c & d) are significantly different at P <0.05

Cholesterol, (TC), triglyceride (TG), high density lipoprotein (HDLc), low density lipoprotein (LDLc), Very low density lipoprotein (VLDLc).

Compared to the normal control negative group, Serum TC, TG, LDLc, VLDLc and T. lipids levels increased significantly in myocardial necrosis control positive group, whereas HDL-cholesterol has been significantly reduced in this group. However, the total cholesterol/ HDLc ratio was also increased significantly. Treated group with flaxseed powder or oil or extract for 60 days showed reduced levels of TC, TG, LDLc, VLDLc and T. lipids and increased HDLc significantly compared to control positive group. The ratio total cholesterol/HDLc was also declined significantly as compared to control positive rat group. Administration of flaxseed either in form of powder, oil and extract caused a significant decrease in serum total cholesterol, LDL-cholesterol, VLDL-cholesterol suggesting beneficial modulator influence on cholesterol metabolism and turnover (table 2).

ISO significantly increased the levels of blood biochemical and hematological parameters when compared to control rats **(Brindha and Rajasekapandiyan 2015)**. Decline in the ratio of total cholesterol/ HDLc observed in the treated rat groups might be a consequence of higher proportion of HDLc that decline the incidence of Atherogenic risk and cardiovascular disease through increased reverse cholesterol transport from peripheral organs to liver and possibly associated with a decrease in intestinal absorption of cholesterol resulting in an increase in fecal excretion of neutral lipids **(Kristensen et al., 2012)**. Also, **Dupasquier et al., (2007)** investigated the anti-Atherogenic capacity of flaxseed in an animal model that represents the human atherosclerotic condition. Supplementation of the cholesterol-enriched diet with ground flaxseed lowered plasma cholesterol and saturated fatty acids, increased plasma content of α-linolenic acid and inhibited plaque formation in the aorta and aortic sinus compared with mice fed a diet supplemented with only dietary cholesterol. Authors demonstrated that dietary flaxseed can inhibit atherosclerosis through a reduction of circulating cholesterol levels and, at a cellular level, via anti-proliferative and anti-inflammatory actions.

Table (3): liver TC, T. lipids and TG of normal control and isoproterenol induced cardiotoxicity rat groups treated with flaxseed powder, oil and extract at the end of the experimental period.

Groups	Liver TC (mg/g)	Liver T. lipids (mg/g)	Liver TG (mg/g)
Control negative	3.41±0.46b	39.66±4.77b	2.61±0.35a
Control positive	7.41±1.19a	60.77±8.11a	1.35±0.23b
Flaxseed powder	3.32±0.39b	41.77±5.11b	2.59±0.31a
Flaxseed oil	3.61±0.43b	42.35±5.21b	2.65±0.33a
Flaxseed extract	3.55±0.45b	38.77±4.22b	2.77±0.42a

Mean values in each column having different superscript (a, b, c & d) are significantly different at P <0.05

Cholesterol (TC) triglycerides (TG**).**

Compared with control negative group, liver TC and T. lipids were significantly increased but TG was significantly decreased in the control positive group. Administration of flaxseed powder, oil and extract at the end of the experimental period attenuated all the isoproterenol induced alterations of these liver lipids diagnostic marker and appeared within normal values as illustrated in table 3.

Abnormal blood lipids, known as dyslipidemias, are one of the major risk factors for heart disease. Flaxseed is reported to reduce the risk of coronary vascular disease because it is a rich source of omega3 fatty acid, dietary lignans, and a class of phytoestrogens and fiber which documented to have lipid lowering and antioxidant properties **(Mozaffarian et al., 2005 and Saman et al., 2011**). Now, Flaxseed meal supplementation may provide a new therapeutic strategy to reduce hypertriglyceridemia and fatty liver **(Bhathena et al., 2002)**.

Table (4): Serum ALT, AST, ALP and LDH of normal control and isoproterenol induced cardiotoxicity rat groups treated with flaxseed powder, oil and extract at the end of the experimental period.

Groups	ALT(µ/ml)	AST(µ/ml)	ALP(µ/ml)	LDH(IU/L)
Control negative	45.77±5.17c	72.33±8.66c	80.77±9.66bc	120.77±14.75c
Control positive	62.11±7.27a	120.77±13.79a	135.75±18.17a	307.33±55.96a
Flaxseed powder	52.11±6.14b	85.11±8.99b	95.77±10.22b	150.33±21.41b
Flaxseed oil	53.71±6.03b	86.77±9.66b	97.14±11.31b	155.77±23.66b
Flaxseed extract	50.71±5.13bc	79.11±9.33bc	93.22±10.05b	143.80±20.11bc

Mean values in each column having different superscript (a, b, c & d) are significantly different at P <0.05

Aspartate aminotransferase (AST), alanine aminotransferase(ALT) alkaline phosphatase(ALP) Lactatet dehydrogenase(LDH).

Compared with control negative group, the activity of serum ALT, AST, ALP and LDH was significantly increased in control positive group. Administration of flaxseed powder and oil at the end of the experimental period could lower these elevation while administration of flaxseed extract reach these serum diagnostic marker enzymes to normal levels as control negative group (table 4).

ALT, AST, ALP and LDH are cytosolic enzymes which serve as diagnostic markers from the damaged tissue into the blood stream. The amounts of these cellular enzymes in the serum reflect the alterations in plasma membrane integrity and/or permeability. Furthermore, the amount of the enzymes appearing in serum is reported to be proportional to the number of necrotic cells, which also reflects a nonspecific alteration in the plasma membrane integrity and/or permeability as a response to β-adrenergic stimulation **(Saravanan et al., 2013)**. In the present study, control positive group showed significant increases in the levels of all these marker enzymes in serum, in line with the results from previous reports, indicating ISO-induced necrotic damage of the myocardium and leakiness of the plasma membrane **(Patel et**

al., 2010). As in our study, **Mueller et al., 2010, Parker et al., 2012 and Tanvir et al., 2015** speculated that antioxidant compounds in flaxseeds preserve liver membrane integrity. Flaxseed is specifically high in the omega-3 polyunsaturated fatty acid which is reported to have significant hepato protective properties.

Table (5): Cardiac XO, LDH and NO of normal control and isoproterenol induced cardiotoxicity rat groups treated with flaxseed powder, oil and extract at the end of the experimental period.

Groups	XO (nmol/mg protein)	LDH (nmol/mg protein)	NO (µmol/mg protein)
Control negative	2.44±0.60c	7.64±1.66bc	11.77±2.04bc
Control positive	15.33±2.76a	36.33±3.78a	60.55±7.22a
Flaxseed powder	4.22±1.11b	9.21±2.11b	14.33±2.67b
Flaxseed oil	4.94±1.03b	9.66±2.14b	15.41±3.11b
Flaxseed extract	4.09±1.08b	9.75±2.13b	14.75±3.10b

Mean values in each column having different superscript (a, b, c & d) are significantly different at P <0.05

Xanthine oxidase (XO), Lactatet dehydrogenase (LDH), Nitric oxide (NO).

Compared with control negative group, the level of cardiac XO, LDH and NO was significantly increased in the isoproterenol control positive group. Administration of flaxseed powder, oil and extract attenuated all the isoproterenol induced alterations of these cardiac diagnostic parameters compared with control positive as well as normalized values of LDH and NO with lowering of XO compared with control negative rat group (table 5).

ISO induces cardiac necrosis by several mechanisms, including increased of oxygen consumption, poor oxygen utilization, increased calcium overload and accumulation, altered myocardial cell metabolism, altered membrane permeability, intracellular acidosis, and increased levels of lipid peroxides. ISO induced heart failure in the rat is associated with nitric oxide dependent, xanthine oxidase (XO) and lactatet dehydrogenase functional alterations of cardiac function **(Krenek et al., 2009 and Lee et al., 2011)**. Also, **Sekine et al., 2007** demonstrated that the oral administration of 1 mL flaxseed oil for 5 days reduces systolic blood pressure and increases prostaglandin and NO release. However, **Karaca and Eraslan 2013** showed that 0.1 ml flaxseed oil administered through gavage for 30 days did not alter nitric oxide levels in the heart, brain and liver of rats. **Omoni and Aluko (2006**) observed that flaxseed protein hydrolysate were able to induce a change of secondary and

tertiary structures of calmodulin, the cofactor involved in the production of nitric oxide responsible for several neurodegenerative diseases.

Table (6): Serum SOD, CAT and MDA of normal control and isoproterenol induced cardiotoxicity rat groups treated with flaxseed powder, oil and extract at the end of the experimental period.

Groups	SOD (µ/dl)	CAT (µ/dl)	MDA(µ/dl)
Control negative	53.66±5.71a	115.77±11.13a	7.55±1.15bc
Control positive	12.33±1.39b	33.67±3.91b	21.14±3.71a
Flaxseed powder	33.66±2.66a	115.99±12.14a	8.11±1.33b
Flaxseed oil	34.20±3.45a	116.33±13.66a	8.41±1.44b
Flaxseed extract	36.77±3.66a	118.71±14.22a	7.96±1.96b

Mean values in each column having different superscript (a, b, c & d) are significantly different at P <0.05

Superoxide dismutase (SOD) malondialdehyde (MDA) Catalase (CAT).

Isoproterenol control positive rat group demonstrated a significant decline in the activity of Serum SOD and catalase as well as a significant rise in the content of MDA in the Serum compared with the control negative group. Administration of flaxseed powder, oil and extract at the end of the experimental period had the potential effect of increase of SOD and catalase levels and attenuating the increase in MDA compared to control positive group (table 6).

MDA is a toxic product of lipid peroxidation but SOD is known to be the primary defense system against oxidative stress. CAT is one of the most important intracellular enzymes in the detoxification of the oxidant hydrogen peroxide. The activity of this enzyme was inhibited due to a high level of toxic metabolites. Earlier studies have demonstrated that during ischemic injury, oxidative stress produced by the generation of reactive oxygen species plays a critical role in the development of myocardial infarction **(Walters et al., 2016)**. It is well established that subcutaneous injection of a high concentration of isoproterenol, a synthetic adrenoceptor agonist, can deplete the energy reserve of the myocardium and induce severe oxidative stress and result in necrotic lesions in the myocardium. The generation of highly cytotoxic free radicals through the autooxidation of catecholamines, has been implicated as one of the important causative factors **(Rathore et al., 1998)**. Isoproterenol could reduce the activity of cardiac biomarkers (creatine kinase–*N*-acetyl-l- cysteine, lactate dehydrogenase, aspartate aminotransferase) and antioxidant markers (superoxide dismutase, catalase, and glutathione) along with significant increase in the level

of malondialdehyde (**Quamrul et al., 2017)**. Epidemiological studies indicate that diets rich in phenols are associated with reduced incidences of several chronic diseases including cardiovascular disease, diabetes and certain types of cancer. Moreover, polyphenols can also bind with bile acids to increase their fecal excretion, which has been hypothesized as a possible mechanism for the lowering of plasma cholesterol levels by polyphenols (**Ngamukote et al., 2011)**. According to **Oomah (2001)** flaxseed contained a peptide mixture with high levels of branched-chain amino acids and low levels of Aromatic Amino Acids. This mixture has shown antioxidant properties by scavenging 2, 2-diphenyl-1-picrylhydrazyl radical (DPPH) and antihypertensive properties by inhibiting the angiotensin I–converting enzyme. Vitamin E, a fat-soluble vitamin in flaxseed, predominantly, in the isomer γ-tocopherol protects cell constituents from the damaging effects of free radicals.

CONCLUSION

Administration of flaxseeds in different form as powder, oil and extract is beneficial in reducing hypercholesterolemia and cardiotoxicity due not only to hypo cholesterolemic effects but also to other potential mechanisms, such as antioxidative, reducing liver lipids and improvement of liver enzymes activity.

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